REMARKS

In response to the Restriction Requirement, Applicants hereby provisionally elect, with traverse, the invention of Group I, claims 1-6 and 32, this group being drawn to a non-competitive immunoassay for a small analyte.

The grounds for traversal are as follows.

The instant application is a 371 National stage application of PCT/FR03/01613, and thus, PCT rules should apply under these circumstances.

PCT Rule § 13.1 states, “The international application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept ("requirement of unity of invention")”. PCT Rule § 13.2 provides that “Where a group of inventions is claimed in one and the same international application, the requirement of unity of invention referred to in Rule § 13.1 shall be fulfilled only when there is a technical relationship among those inventions involving one or more of the same or corresponding special technical features. The expression "special technical features" shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art”. Thus, the requirement is art-based.

Applicants respectfully traverse the Examiner’s objection for absence of a common technical feature among Groups I, II and III. Applicants submit that the Official Action fails

to satisfy the requirements of PCT Rule § 13.1 and PCT Rule § 13.2.

The Examiner takes the position that the claims lack unity of invention because the technical feature therein is not a contribution over the prior art as referenced by SELF et al. (Clinical Chemistry, Vol. 40, No. 11, pages 2035-1041, 1994). In this regard, the Office argues that SELF teaches a dual antibody reagent-pair applicable to noncompetitive immunometric assay systems. Applicants respectfully disagree.

The assay described in SELF is based on the interaction of a receptor, such as a primary antibody, with its ligand, such that new binding sites recognizable by a secondary antibody are formed. SELF further details a digoxin assay utilizing an anti-complex antibody that recognizes a digoxin-bound primary antibody with affinity >2000-fold over its binding to the primary antibody alone (*see,* SELF et al., Abstract). SELF discloses that the secondary monoclonal antibodies, reactive against the Ab1-digoxin complex, were raised by administering immunogen (Ab1-digoxin) to mice and eventually selecting for hybridomas producing antibodies that bound preferentially to the Ab1-digoxin immune complex. SELF fails to teach or suggest, however, an immunoassay system wherein the second binding partner is obtained from a <u>non-immunized source</u> which is a <u>naïve display recombinant binding partner library</u>, as featured in all of instant claims 1-6, 18-20 and 26-33.

Non-competitive immunoassays have many advantages over competitive immunoassays, such as improved speed, sensitivity and specificity. A non-competitive immunoassay is based on the use of two antibodies that bind to two different epitopes of the antigen. This works well for high molecular weight analytes, but when the analyte is small (as in the instant claims) there is not enough space for binding the two different antibodies. Still there are some publications, e.g., SELF et al., that disclose non-competitive assays for small analytes. In these assays a secondary anti-immune complex (anti-IC) antibody is used, which binds to the immune complex formed by the primary anti—analyte antibody and the antigen, but not to the analyte or the primary antibody alone. The difficulties, however, lay in obtaining the appropriate secondary anti-IC antibody. The immune complex used for immunization tends to break down before the response to the immune complex is obtained.

The present invention overcomes this problem. More specifically, in the last paragraph starting at the bottom of page 2, the specification discloses that the present invention provides an immunoassay that circumvents immunization of animals with an immune complex (IC), which can be extremely difficult. At page 3, lines 6-9, the specification discloses that the difficulties associated with raising anti-IC antibodies can be avoided by providing the necessary anti-IC antibodies from a display recombinant binding partner library, instead of from

immunized animals. Thus, according to the present invention, the desired second binding partner of the claims is obtained from a non-immunized source. The desired second binding partner is obtained from a naive binding partner library as set forth, for example, at page 8, line 24, and as illustrated at page 14, Example 1.

The Office Action further takes the position that it is well known in the art that antibodies can also be produced from a recombinant library (e.g., ARAI et al., Protein Engineering, Vol. 13, No. 5, pages 369-376, 2000). The Office Action fails to recognize, however, that the use of a naive recombinant binding partner library provides a complete solution to the problems associated with immunizing with an immune complex. The use of a naive recombinant binding partner library, as featured in instant claims 1-6, 18-20 and 26-33, further defines the invention over the art.

Contrary to the position taken in the Office Action, SELF and ARAI fail to teach or suggest the special technical feature of the present invention - a noncompetitive immunoassay that utilizes a dual antibody reagent pair wherein one of the antibodies is obtained from a non-immunized source that is a naïve display recombinant library.

Applicants also respectfully disagree with the position taken in the Office Action that the claims of Group I, II and III are drawn to three independent inventions.

In particular, referring to Groups I and III, the claims of both groups are directed to a non-competitive immunoassay for small analytes employing a reagent pair of which the second binding partner is obtained from a non-immunized source, which is a naïve display recombinant binding partner library. The only difference between Groups I and III is that in Group III the reagent pair is specified by indicating the particular amino acid sequences. More specifically, in independent claim 26, the second binding partner comprises a ligand binding portion of K11 scFv comprising SEQ ID NO: 5; in independent claim 27, the first binding partner comprises a ligand-binding portion of M1 Fab comprising SEQ ID NO: 1 and SEQ ID NO: 2, or of M2 Fab comprising SEQ ID NO: 3 and SEQ ID NO: 4.

The claims of Group III (26-31) could in fact be redrafted into claims dependent from claim 1. Indeed, the Office Action dated April 29, 2008 indicated that claims 26-31 contained allowable subject matter. Consequently, Applicants amended claims 26 and 27 to independent form including all of the limitations of the base claim (claim 1). The Office now alleges that these claims are now drawn to independent inventions.

Referring to Group II, the claims of Group II also relate to the same inventive concept as the claims of Groups I and III. The common inventive concept is the surprising finding that appropriate second binding partners that recognize a complex of analyte and first binding partner can be obtained from a non-

immunized source, whereby no immunization with an immune complex is required.

For all of the above reasons, Applicants respectfully submit that the teachings of SELF, along with any other teachings in the art, are insufficient, such that SELF cannot teach or suggest each and every element of the claims. Accordingly, the prior art fails to teach or suggest the special technical feature of the present claims, and restriction between Groups I, II and III is improper.

Thus, in view of the above, Applicants respectfully submit that the present claimed invention is a contribution over the prior art and that unity of invention for Groups I, II and III should be recognized. As a result, Applicants believe that the Official Action fails to satisfy its burden in showing that the claims lack a special technical feature.

Therefore, Applicants believe that all of the claims are sufficiently related so as to warrant a search and examination of all the claims in their full scope. Such action is respectfully requested at this time.

In the event that the Office disagrees with the traversal and maintains the Restriction requirement, then kindly consider the possibility of rejoinder of the non-elected subject matter, upon a determination of allowance of the election invention, per U.S. practice and M.P.E.P. § 821.04.

Favorable action on the merits is solicited.

Should there be any matters that need to be resolved in the present application, the Examiner is respectfully requested to contact the undersigned at the telephone number listed below.

The Commissioner is hereby authorized in this, concurrent, and future submissions, to charge any deficiency or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

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